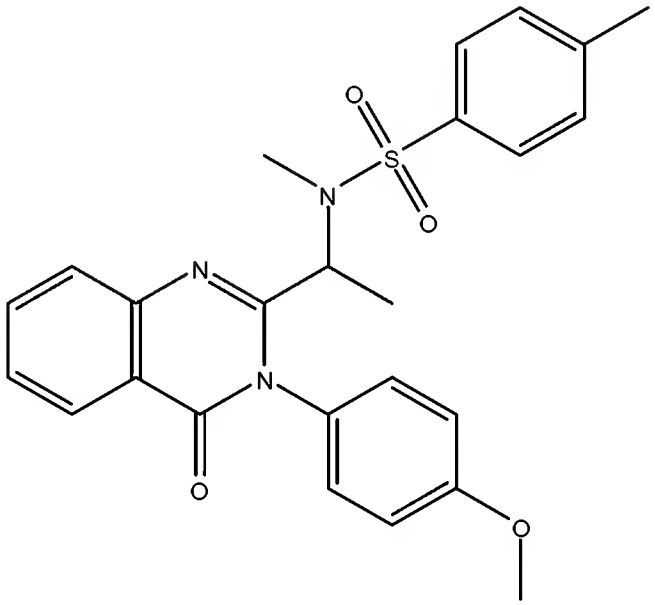
REMARKS

Claim Rejections under 35 U.S.C. § 112, Second Paragraph

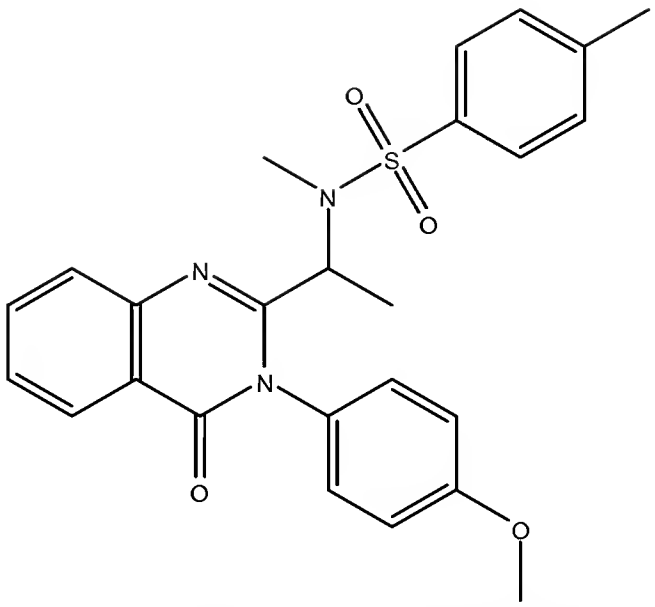
1. The Office rejected claim 5 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as their invention. The Action states that only the first three species of claim 5 belong to the subspecies of formula III. Applicants respectfully disagree, based on the structures of the species as established with the *Chemdraw* software program.

Choosing species randomly, the fifth listed species in claim 5 is



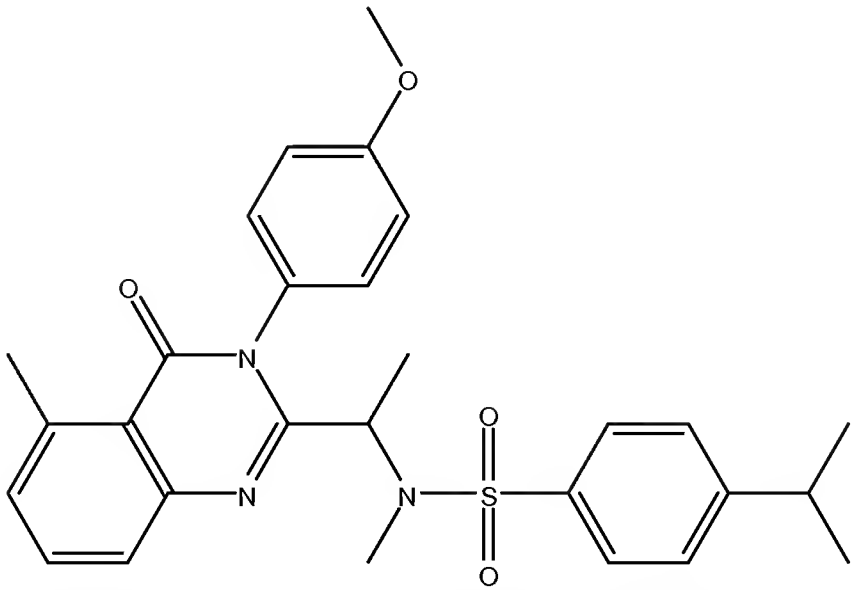
N-{1-[3-(4-methoxyphenyl)-4-oxo-3,4-dihydroquinazolin-2-yl]ethyl}-4,N-dimethylbenzenesulfonamide

The tenth listed species in claim 5 is



N-{1-[3-(4-methoxyphenyl)-4-oxo-3,4-dihydroquinazolin-2-yl]ethyl}-4,N-dimethylbenzenesulfonamide

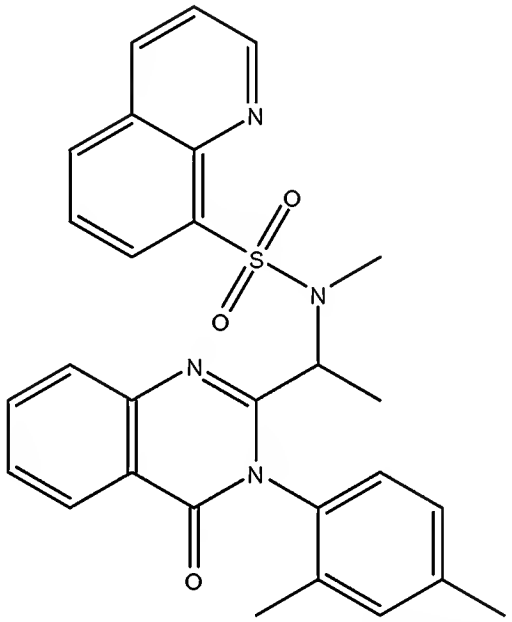
and the fifteenth listed species in claim 5 is



4-isopropyl-N-{1-[3-(4-methoxyphenyl)-5-methyl-4-oxo-3,4-dihydroquinazolin-2-yl]ethyl}-N-methylbenzenesulfonamide

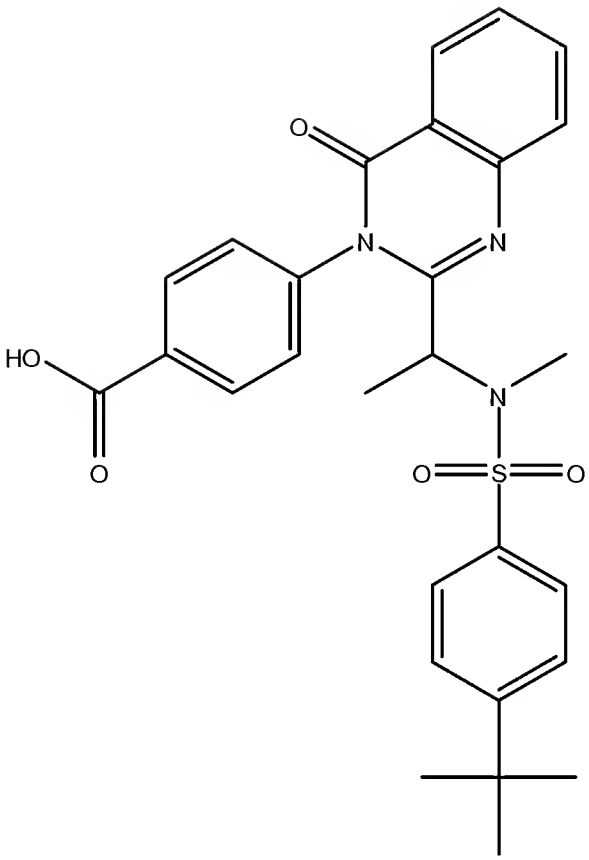
It is respectfully requested that the Examiner specifically point out which aspect of these structures does not fall within the definition of Formula III as set forth in claim 3, and particularly identify the particular limitations of claim 3 that are not met by these structures.

2. Similarly, claims 7, 11, and 101 are rejected as allegedly failing to fall within the scope of claim 3. As to claim 7, the first species is



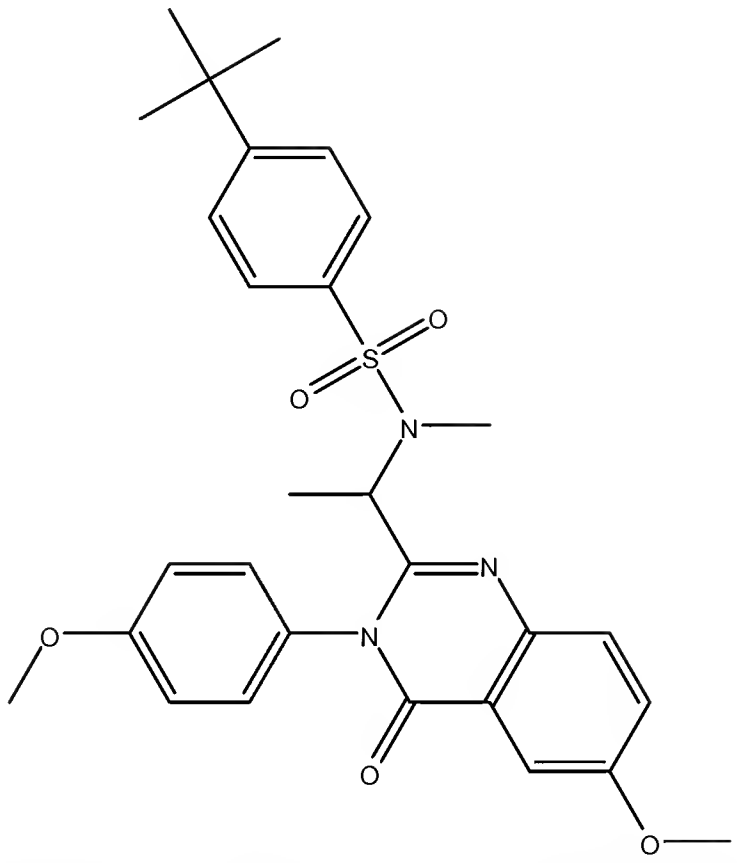
quinoline-8-sulfonic acid {1-[3-(2,4-dimethylphenyl)-4-oxo-3,4-dihydroquinazolin-2-yl]ethyl}methylamide

As to claim 11, the first species is



4-(2-{1-[(4-tert-butyl-benzenesulfonyl)methylamino]ethyl}-4-oxo-4H-quinazolin-3-yl)-benzoic acid

As to claim 101, the first species is



4-tert-butyl-N-{1-[6-methoxy-3-(4-methoxyphenyl)-4-oxo-3,4-dihydroquinazolin-2-yl]ethyl}-N-methylbenzenesulfonamide

Again, it is respectfully requested that the Examiner particularly point to the structures of these compounds alleged not to fall within the scope of claim 3, previously presented, and point to the limitations of claim 3 that are not met by these structures.

As it is respectfully submitted that all of the named compounds do in fact fall within the scope of claim 3, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

C. Claim Rejections under 35 U.S.C. § 103(a)

Claims 3-7, 10, 28, 30, 31, 33, 34, 36, 37, 39, 50, 99, and 101 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Baxter et al. (US 6,545,005 B1) (Baxter). Applicants respectfully traverse this rejection.

On page 4 of the Office Action the Office has asserted that generic formula II of Baxter encompasses the instant formula III. The Office has further asserted that although Baxter does not disclose additional species of a sulfonamide substituent at the 2-position, the formula II subgenus in column 31 provides sufficient teaching for one skilled in the art to select compounds of the instant formula III to agonize or antagonize hedgehog pathway. Applicants respectfully disagree and submit that the present claims would not have been obvious over Baxter.

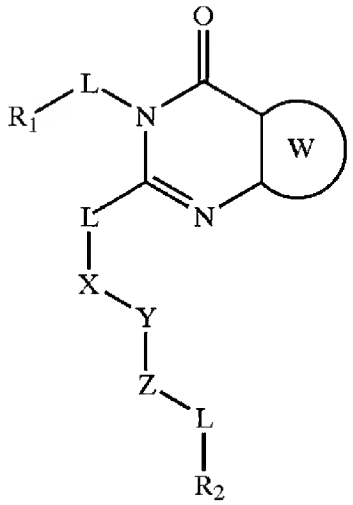
The rejection seems to be based on the concept that a species cannot be patentable over a prior art genus. That is incorrect. It is well settled that a valid patent may issue for a non-obvious improvement on a prior patented invention even if the improvement falls within the claims of that prior patent. *Corning Glass Works v. Sumitomo Electric U.S.A.*, 868 F.2d 1251, 1262, 9 USPQ2d 1962, 1970 (Fed. Cir. 1989). "[A] 'genus patent' does 'not estop [an] applicant from later filing an improvement patent …to claim species with particularly useful properties." *Integra Lifescience I, Ltd. V. Merck KGaA* (331 F.3d 860, 869, 66 USPQ2d 1865 (Fed. Cir. 2003) rev's and remanded 545 U.S. 193 (2005). See also *Eli Lilly & Co. v. Board of Regents of the University of Washington*, 334 F.3d 1264, 1270, 67 USPQ2d 1161 (Fed. Cir. 2003) *cert denied*, 541 U.S. 968 (2004), stating an "earlier disclosure of a genus does not necessarily prevent patenting a species member of the genus. *See, e.g. Bristol-Myers Squibb Co. v. Ben Venue Labs, Inc.*, 246 F.3d 1368, 1380 (Fed. Cir. 2001)."

The fact that a claimed compound may be encompassed by a disclosed generic formula does not by itself render that compound obvious. *In re Jones*, 958 F.2d 347, 350, 21 USPQ2d 1941,1943 (Fed. Cir. 1992). Particularly instructive is the case of *In re Baird*, 16 F.3d 380, 29 USPQ2d 1550 (Fed. Cir. 1994), wherein the court considered the patentability of claims to three particular species over a prior art reference that disclosed millions of compounds, including those of the applicant's claims. The court noted that while the formula of the reference unquestionably encompassed the claimed compounds when specific variables were chosen, there was nothing in the disclosure of the reference suggesting that one should select such variables. The court also noted that the reference suggested that compounds other than those that were the subject of applicant's claims were preferred. Where the reference failed to suggest that the applicant's claimed compounds were preferred, and offered no motivation for the selection of the claimed compounds, the applicant's claims were found to be non-obvious and patentable.

Here, as in *Baird*, there is nothing in the cited Baxter reference directing one to the presently claimed subgenus of compounds, nor is there any suggestion that such compounds would be effective nuclear receptor modulators in general or farnesoid X receptor (FXR) modulators, in particular. The presently claimed genus of compounds is but a small subgenus of the genus disclosed in col. 31 of Baxter, as manifested in the following recitation from col. 31 of Baxter in which the moieties other than those recited by the Office are displayed as strikethrough text:[1]

In embodiments wherein Y_1 and Z_1 are absent and X_1 comprises a pyrimidone, compounds useful in the present invention may be represented by general formula (II):

Formula II



wherein, as valence and stability permit,

R_1 represent[s] ~~H, lower alkyl,~~ aryl (e.g., substituted or unsubstituted)~~, aralkyl (e.g., substituted or unsubstituted, e.g., $-(CH_2)_n$-aryl), or heteroaryl (e.g., substituted or unsubstituted), or heteroaralkyl (e.g., substituted or unsubstituted, e.g., $-(CH_2)_n$ heteroaralkyl -)~~;

R_2[, represents ~~H,~~ lower alkyl, aryl (e.g., substituted or unsubstituted)~~, aralkyl (e.g., substituted or unsubstituted, e.g., $-(CH_2)_n$-aryl), or heteroaryl (e.g., substituted or unsubstituted), or heteroaralkyl (e.g., substituted or unsubstituted, e.g., $-(CH_2)_n$ heteroaralkyl -)~~;]

L, independently for each occurrence, is absent or represents ~~$-(CH_2)_n$- alkyl, -alkenyl -, -alkynyl -, $-(CH_2)_n$-alkenyl -, $-(CH_2)_n$-alkynyl -, $-(CH_2)_n$-$O(CH_2)_p$-, -~~ $(CH_2)_nNR_2(CH_2)_p$-;

X can be selected from ~~$-N(R_8)$-, -O-, -S-, -Se-, -N=N-, -ON=CH-, $-(R_8)N$-$N(R_8)$-, $-ON(R_8)$-, a heterocycle, or~~ a direct bond between L and Y;

[1] R_1 and R_2, which are defined in Baxter identically but independently of each other has been split into two paragraphs for clarity.

Y can be selected from ~~-C(=O)-, -C(=S)-, $S(O_2)$-, -S(O)-, -C(=NCN)-, -P(=O)(OR_2)-, a heteroaromatic group, or a direct bond between X and Z~~;

Z can be selected from ~~-N(R_8)-, -O-, -S-, -Se-, -N=N-, -ON=CH-, -R_8-N-NR_8-, -ONR_8-, a heterocycle, or~~ a direct bond between Y and L;

~~R_8, independently for each occurrence, represents H, lower alkyl, aryl (e.g., substituted or unsubstituted), aralkyl (e.g., substituted or unsubstituted, e.g., -$(CH_2)_n$-aryl), or heteroaryl (e.g., substituted or unsubstituted), or heteroaralkyl (e.g., substituted or unsubstituted, e.g., -$(CH_2)_n$-heteroaralkyl-), or two R_8 taken together may form a 4- to 8-membered ring, e.g., with X and Z, which ring may include one or more carbonyls;~~

W represents a substituted or unsubsituted [sic] aryl ~~or heteroaryl~~ ring fused to the pyrimidone ring;

p represents~~, independently for each occurrence, an integer from 0 to 10, preferably from 0 to 3~~;

and n, ~~individually for each occurrence,~~ represents ~~an integer from 0 to 10,~~ preferably from 0 to 5.

As is apparent from the foregoing, the presently claimed genus of compounds is but a small subgenus of compounds encompassed by the description in col. 31 of Baxter and, indeed, is even a subgenus of the subgenus identified by the Office as R_1. R_2, and W can each be "substituted," but no specific substituents are identified.

There is nothing in Baxter giving reason to one of ordinary skill in the art to select such compounds. Baxter discloses but a single compound having a sulfonamide linkage (compound 14, spanning cols. 75-76) falling within the subgenus identified by the Office, but presents it merely as a synthetic example and does not otherwise identify it as being of particular interest. Significantly, this compound is not among those identified in the assay presented in col. 63 of Baxter. As recently reiterated in *Bayer Schering Pharma AG v. Barr Laboratories Inc.*, 91 USPQ2d 1569, 1573 (Fed. Cir. 2009), generalities or vague or non-existent guidance towards the claimed invention is insufficient to render a claim obvious; there must be some reason for the ordinary artisan to make the *particular* invention being claimed. Baxter provides no reason for one of ordinary skill in the art to select the particular subgenus of compounds presently being claimed.

In addition, Baxter fails to provide information from which one of ordinary skill in the art could expect that the presently claimed compounds would be nuclear receptor modulators or, in particular, FXR modulators. Baxter only discloses the use of small molecule compounds that agonize inhibition of hedgehog signaling in the regulation of repair and/or functional

performance of a wide range of cells, tissues and organs having the phenotype of hedgehog gain-of-function. The mechanism of action of Baxter compounds of formula II is specific to signal transduction pathways regulated by a hedgehog family of genes, and only speculatively attributed to an activation of a hedgehog receptor. No utility or even potential utility was disclosed or suggested for Baxter compounds of formula II for use as quinazolinone modulators of nuclear receptors in general and (FXR) in particular, as disclosed in the present application. Thus, the properties of the presently claimed compounds as FXR modulators could not have been predicted from Baxter.

Without reason to select the presently claimed compounds or the ability to predict their properties as nuclear receptor/FXR modulators, the presently claimed compounds cannot be obvious.

The examiner's indication that claim 100 would be allowable if rewritten in independent form is noted with appreciation, however it is respectfully submitted that such an amendment is not necessary in view of the arguments above.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

D. Non-Elected Subject Matter

As method claims 84-98 as presented require all the limitations of the elected product (compound) claims which are allowable as indicated above, the Applicants respectfully request their rejoinder.

In light of the all above arguments, Applicants respectfully request reconsideration and withdrawal of the rejections of the pending claims. If the Examiner believes it to be helpful, he is invited to contact the undersigned representative as indicated below.

Respectfully submitted,

Date: July 27, 2010

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